

Conference on Cellular and Molecular Studies in Bone Marrow Transplantation

Chairperson: Brian R. Smith

Vice-Chair: Steven J. Burakoff

To be held: July 16-21, 1989 at the Vermont Academy, Saxtons River, Vermont

Tentative Schedule of Sessions

Each session will consist of a 15-20 minute introduction/presentation by the discussion leader followed by four different presentations, each 30 minutes with 10 minutes of questions following.

Monday, A.M.

The Role of the Major Histocompatibility Complex in Transplantation Biology

Discussion Leader (and Speaker): John A. Hansen, Professor of Medicine, Univ of Washington, and Member, Fred Hutchinson Cancer Research Center, 1124 Columbia Street, Seattle, WA 98104 (The MHC in Human Transplantation)

Speakers:

Jack Strominger, Prof of Biochemistry and Molecular Biology, Harvard University, 7 Divinity Avenue, Cambridge, MA 02138 (Human HLA Structure and Function)

David H. Sachs, Chief, Immunology Branch, National Cancer Institute, NIH Bldg 10 Rm 4B17, Bethesda, Maryland 20892 (Transplantation across HLA Barriers in Animal Models)

Richard A. Flavell, Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT (Murine H-2 Structure and Function)

Monday, P.M.

T and NK Cell Ontogeny and Function

Discussion Leader (and Speaker): Steven J Burakoff, Prof of Pediatrics, Harvard Medical School, Dana-Farber Cancer Institute, 44 Binney Street, Boston, MA 02115 (T Cell Recovery Post Transplant)

Speakers:

Jeffrey Ledbetter, Senior Scientist, Dept of Immunology, Oncogene Corporation, 3005 First Avenue, Seattle, Washington 98121 (Mechanisms of T cell Activation)

Samuel Strober, Prof of Medicine, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94305-5111 (Specific Suppressor Cells Following Transplantation)

Richard G Miller, Prof of Immunology, University of Toronto, Medical Sciences Bldg, Toronto, Ontario, Canada M5S 1A8 (T Cell Ontogeny)

Tuesday, A.M.

Graft Rejection

Discussion Leader (and Speaker): Richard O'Reilly, Prof of Pediatrics, Cornell University Medical School, Memorial-Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York 10021 (Experience in Human T Cell Marrow Manipulation)

Speakers:

Michael Bennett, Prof of Pathology, Univ of Texas Health Sciences Center, 5323 Harry Hines Blvd, Dallas, TX 75235 (Natural Killer Cells and Graft Rejection)

J Joachim Deeg, Georgetown University School of Medicine, Lombardi Cancer Research Center, 3800 Reservoir Road NW, Washington, DC 20007 (Ultraviolet Irradiation and Canine Transplantation Models)

Gunther Dennert, Assoc Prof of Microbiology, NOR 620, USC Medical School, 2025 Zonal Avenue, Los Angeles, CA 90033 (Mechanisms of Graft Rejection)

Tuesday P.M.

Graft Versus Host Disease

Discussion Leader (and Speaker): Robertson Parkman, Prof of Pediatrics, University of Southern California, Los Angeles Children's Hospital, PO Box 54700, Los Angeles, CA 90054-0700 (Murine Models of Chronic and Acute GVHD)

Speakers:

Alfred D Steinberg, Chief, Cell Immunology Arthritis and Rheumatism Branch, NIAMS, NIH Bldg 10 Rm 9N218, Bethesda, MD 20892 (Regulation of Autoimmunity)

Daniel A Vallera, Associate Professor of Therapeutic Radiology, Univ Minnesota, Box 367 UMHC, 420 Delaware St, SE, Minneapolis, Minnesota 55455 (T Cell Marrow Manipulation)

Robert Korngold, Wistar Institute, 36th Street at Spruce, Philadelphia, PA 19104 (Murine Models of Graft Versus Host Disease)

Wednesday, A.M.

T and Accessory Cells Post Transplant

Discussion Leader: Jordan Pober, Assoc Prof of Pathology, Harvard Medical School, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115 (Endothelial Cell Biology in Transplantation)

Speakers:

Irving L Weissman, Prof of Pathology, Stanford University School of Medicine, Stanford, CA 94305 (The MHC and Immune Ontogeny)

Barton F Haynes, Prof of Medicine, Duke University Medical Center, Box 3258, Duke Hospital, Durham, NC 27710 (T Cell Ontogeny)

Raef S Geha, Associate Prof of Pediatrics, Dept of Allergy, Children's Hospital Medical Center, 300 Longwood Avenue, Boston, MA 02115 (Accessory Cell Interactions Post Transplant)

Wednesday, P.M.

Regulation of Hematopoiesis: Growth Factors and Stromal Cells I

Discussion Leader: David G. Nathan, Prof of Pediatrics, Harvard Medical School, The Childrens Hospital, 300 Longwood Avenue, Boston, MA 02115 (GM-CSF)

Arthur W Nienhuis, Chief, Clinical Hematology Branch, National Heart Lung and Blood Institute, 9000 Rockville Pike, NIH Bldg 10 Rm 7D19, Bethesda, MD 20892

Michael Dexter, England (stromal cells)

David W. Golde, UCLA Center for Health Sciences, Division of Hematology-Oncology, Los Angeles, CA 90024

Malcolm A.S. Moore, Member and Professor, Sloan Kettering Institute for Cancer Research, New York, NY 10021 (G-CSF)

Thursday, A.M.

Gene Transfer Therapy

Discussion Leader (and Speaker): David Williams, Pediatric Oncology, Dana-Farber Cancer Institute and Children's Hospital, Boston, MA

Speakers:

Dusty Miller, University of Washington, Seattle, WA (Retroviral Vectors for Gene Transfer Therapy)

Elio Gilboa, Memorial Sloan-Kettering Cancer Institute, 1275 York Avenue, New York, NY 100 (Primate Models of Gene Transfer Therapy)

Richard C Mulligan, Whitehead Institute, Cambridge, MA (Gene transfer into keratinocytes)

Thursday, P.M.

B Cell Ontogeny and Regulation

Discussion Leader: Brian R Smith, Assoc Prof of Internal Medicine, Laboratory Medicine, and Pediatrics, Yale University School of Medicine, 333 Cedar Street, New Haven, CT 06510

Owen Witte, Assoc Professor of Microbiology, UCLA, 405 Hilgard Avenue, Los Angeles, CA 90024 (Regulation of B Cell Development)

Abul K Abbas, Assoc Prof of Pathology, Harvard Medical School, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115 (Murine Models of B Cell Reconstitution post transplant)

Lee Nadler, Dana-Farber Cancer Institute, 45 Binney Street, Boston, MA 02115 (B Cell Reconstitution Post Human Transplant)

Peter E Lipsky, Prof of Internal Medicine and Microbiology, Univ of Texas Health Sciences Center, 5323 Harry Hines Blvd, Dallas, TX 75235

Friday, A.M.

Regulation of Hematopoiesis: Growth Factors and Stromal Cells II

Discussion Leader (and Speaker): Curt I. Civin, Johns Hopkins Hospital, Baltimore, Maryland

Joel S. Greenberger, Department of Radiation, University of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, MA 01605 (Stromal Cell Biology in Transplantation)

James D. Griffin, Dana-Farber Cancer Institute, 44 Binnet Street, Boston, MA 02115 (Myeloid Growth Factor Regulation)

**Background and Format of the Conference**

The Federation of American Societies of Experimental Biology (FASEB) has sponsored Summer Research Conferences since 1982. Because of recently increasing strong interest in the field of basic studies in bone marrow transplantation, the scientific Advisory Committee of FASEB decided to include a Summer Research Conference on "Cellular and Molecular Studies of Bone Marrow Transplantation" for the 1989 Conferences, to be held the week of July 16-21, 1989 in Saxtons River, Vermont. The topic is of interest to scientists of many disciplines including molecular biology, cellular immunology, developmental biology, pharmacology, biochemistry, and radiation biology. This multi-disciplinary interest arises out of the unique model system which marrow transplantation presents, that is, the recapitulation of immune and hematopoietic ontogeny in settings of syngeneic donor-recipient combinations as well as minor and major histocompatibility mismatched donor-recipient combinations and in the presence or absence of a functional thymus. Thus the topic is not only of intrinsic interest but also provides an excellent forum for scientists of somewhat diverse backgrounds to discuss areas of common ground.

The major current conference on the topic of bone marrow transplantation per se is the UCLA Symposium on Marrow Transplantation which is held every other year, generally in Colorado or Utah. That conference was most recently held in Spring, 1988 and is scheduled again for Spring, 1990. The UCLA Conference is more clinically oriented than the FASEB Conference will be. Scheduling a FASEB summer conference on the East Coast that is oriented toward unpublished basic research (i.e., Gordon Conference style) related to the broad field of marrow transplantation and held in the years alternate to the UCLA Conference is therefore likely to complement the UCLA Conference rather than overlap with it. The UCLA Conference which attracts more than 300 participants is routinely oversubscribed and we believe therefore that the Summer FASEB Conference is likely to attract approximately 1/3 of the participants in the UCLA conference plus an additional 50 basic scientists who might not be interested in the clinically oriented portions of the UCLA Conference. There are a number of other meetings during the year which include transplantation related material (including the American Society of Hematology, the FASEB meetings themselves, and the European and American transplantation meetings) as well as some very specialized small meetings on areas of practical and research transplantation biology (for example, meetings on methods of bone marrow purging). However, none of these meetings utilizes the Gordon Conference format, nor are they exclusively dedicated to areas of related basic science research in the field. The FASEB Conference has been scheduled so as to immediately precede that of the Seventh International Congress of Immunology to be held in Berlin from 30 July to 5 August, 1989 so as to not only avoid potential conflict with that meeting but also to provide an easy route for scientists interested in both conferences to attend the Vermont FASEB conference on their way to the International Congress.

The format of the FASEB Conference will parallel that of the Gordon Conferences because that format has proven to be exceptionally conducive to scientific communication and interchange. The scientific sessions are specifically forbidden to be recorded and are unpublished in order to encourage as much as possible the presentation of the most recent results and to stimulate free information

exchange. In addition to the formal presentations and discussion sessions, the fact that participants share living quarters, meals, and recreational facilities encourages even greater informal exchange of data.

There will be nine major scientific sessions held from 9 am to noon and 7 pm to 10 pm daily (except Friday for which only the morning session is held). A detailed tentative list of invited speakers and topics is included at the end of the text. Each session will have a discussion leader whose task it will be to briefly present a conceptual background defining the current state of knowledge and major questions for a given topic area. That individual will then introduce the speakers and, along with the conference chairperson and vice-chairperson, take responsibility for stimulating discussion among both the speakers and the participants. All of the invited discussion leaders will have significant experience in carrying out these objectives. A deliberate attempt is made in this conference to include several different but related scientific topics and disciplines, all bound together in the common area of marrow transplantation research. The use of discussion leaders is expected to provide sufficient background information so that all participants will become familiar with related areas of investigation and participate actively in the discussions regardless of their particular specialty backgrounds. Four major speakers will be scheduled for each session. Each will give approximately a one-half hour talk, with the remaining time devoted to discussion. In some cases the discussion leader will also give one of the principal talks.

Afternoons are left open for informal discussion among participants as well as informal poster sessions. Workshops, especially in areas of multidisciplinary interest, will also be scheduled either at the meeting or in advance based on the interests of the participants. The use of afternoon time for these informal sessions will encourage younger scientists to discuss their results and plans with senior researchers in a spontaneous and unpretentious format.

The program of the Conference will be published several months in advance in the FASEB Journal, Science, and the major publications of the relevant constituent societies of FASEB. We expect to also publish the schedule in the journals Blood, Transplantation, and Cell to reach the widest appropriate multidisciplinary audience. Applicants will be selected based on their scientific accomplishments to ensure excellence and to foster multidisciplinary interactions. In determining attendance, the Chairperson and Vice-Chairperson will also consider geographic and institutional distribution. Consideration will especially be given to younger investigators showing interest and potential in disciplines related to marrow transplantation to promote the field's progress by bringing in new and enthusiastic scientists.

Based on the considerations outlined above, we anticipate that the maximum number of participants (150) will be invited. Housing and dining facilities will be provided at the Conference Center at the Vermont Academy in Saxtons River, Vermont. The fee for the Conference, including registration, lodging, and meals will be approximately \$325 per person. Logistic support will be provided by the FASEB staff, including those at the conference site as well as those at the main FASEB offices for handling related paperwork and accounting. Sessions will be conducted in a comfortable auditorium equipped with modern audio-visual facilities. Both the Chairperson and Vice-Chairperson have experience in organizing both conferences and courses that attract a national and international audience.

The major areas of intense inquiry in marrow transplantation in 1988 include the following interacting concerns: (1) What are the molecular and cellular mechanisms by which major and minor histocompatibility antigens determine the interactions of immunocytes?; (2) What are the cellular and molecular mechanisms by which T cells, NK cells, and B cells are activated?; (3) What is the normal ontogeny of the hematopoietic and immune systems following transplantation, both in a thymic and athymic setting and how is that development regulated?; (4) How can graft versus host disease and graft rejection be abrogated so as to result in a tolerant host-donor relationship?; (5) What are the molecular biological, immunological, and hematopoietic developmental manipulations that will need to be carried out if gene transfer therapy in man is to become an eventual reality? Each of these questions has both basic scientific interest in our understanding of the human organism and also

potential pragmatic importance in medical therapeutics. In particular, further knowledge of the answers to the first question could result in the application of clinical allogeneic marrow grafting to a larger number of potential patient recipients by expanding the donor pool; answers to the second and third questions may provide clues to clinical strategies that would result in reducing the morbidity and mortality of clinical grafting that is due to the often profound failure of normal immune and hematopoietic reconstitution after transplant (e.g., infections, secondary tumors); answers to the fourth question have direct applicability to man and answers to the fifth would, of course, bring us closer to realistic gene transfer therapeutics.